

REMARKS

New claims 42-43 have been added. Support for the new claims can be found throughout the present specification, for example, at page 3, lines 31-39.

Claims 22-43 are pending in the application, with claims 22, 28, 42 and 43 being the independent claims.

**I. The Rejection of Claims 2, 4 and 6-7 Under 35 U.S.C. § 112, First Paragraph
Should be Withdrawn**

Claims 22-41 have been rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. Applicant respectfully traverses this rejection.

The Office Action suggests that support for the phrase “and wherein the at least one first detector and the at least one second detector are fixedly arranged as a rigid arrangement,” and specifically “rigid arrangement,” are not found in the specification. Applicant respectfully disagrees.

Applicant submits that support for the phrases “and wherein the at least one first detector and the at least one second detector are fixedly arranged as a rigid arrangement,” and “rigid arrangement” can be found throughout the present specification. For example:

The entire *rigid arrangement* combined in the housing 15 (CCD cameras 1, 2, reflectors 27, 28, lenses 25, 26, masks 23, 24 and SPECT detectors 19, 20) can be rotated about the tube 9, preferably through 360°, in order to be able to obtain a series of measurement data at identical angular distances all around the subject to be examined.

Present Specification at page 10, lines 16-20 (emphasis added).

Applicant respectfully submits that the present specification clearly provides explicit written description support for the phrases “and wherein the at least one first detector and the at least one second detector are fixedly arranged as a rigid arrangement,” and “rigid arrangement.”

In view of the foregoing remarks, Applicant respectfully requests reconsideration and withdrawal of the rejection under 35 U.S.C. §112, first paragraph.

II. The Rejection of Claims 22 and 28 Under 35 U.S.C. § 103 Should be Withdrawn

Claims 22 and 28 have been rejected under 35 U.S.C. § 103(a), as allegedly being unpatentable over U.S. Patent No. 6,280,703 to Combs *et al.* (hereafter "Combs"), in view of U.S. Patent No. 4,969,175 to Nelson *et al.* (hereafter "Nelson"). Applicant respectfully traverses this rejection.

The Office Action suggests that Combs discloses an imaging method comprising simultaneously determining *in vivo* distributions of bioluminescent and/or fluorescent markers and radioactive markers utilizing a first and second detector. The Office Action indicates that Combs discloses that the first and second detectors are arranged in a specific spatial arrangement relative to each other.

The Office Action concedes, however, that Combs fails to disclose that the detectors are placed at identical projection angles, and relies on the disclosure of Nelson to cure this deficiency. Specifically, the Office Action suggests that Nelson, in the field of multiple energy x-ray imaging, discloses imaging at two different energy levels at the same projection angle. The Office Action concludes that it would have been obvious to determine the distributions of the markers at the same projection angle in order to properly compare the detected energies relative to the part being imaged. Applicant respectfully disagrees with these contentions and conclusions.

Applicant respectfully submits that, contrary to the assertions in the Office Action, Combs does not disclose an imaging method as set forth in the presently claimed invention. Rather, Combs is directed to detection of the *presence* of "tracers" in a body fluid. *See* Combs at column 5, lines 14-16. ("The detection of the tracers can be achieved by radiometric, magnetic, ultrasonic, or optical methods known in the art.") Applicant submits that a person of ordinary skill in the art would clearly understand that a method of *detecting the signal* from a tracer is not the same as a *method of imaging*. In fact, the term "imaging" never appears in the specification of Combs.

Simply because Combs discloses that its methods are capable of "assessing organ function" by detecting the signal from a tracer in a body fluid, there is no indication that the

method would be capable of imaging. The data generated by the method of Combs simply provides a time course of signal intensity values. *See, e.g.*, Combs at Figures 2-4. Combs provides no imaging data utilizing the disclosed method. As set forth in the present specification, “[t]he present invention is preferably used for *in vivo* studies of small animals (for example mice or rats), for *in vivo* observation of gene expression and for breast, prostate, skin tumor and thyroid gland imaging.” Present Specification at page 7, lines 20-22. Applicant respectfully submits that there is no reason to believe that the method of Combs could in any way be utilized as the presently claimed method for the imaging of breast, prostate, skin tumor or thyroid gland.

Applicant submits that this deficiency in Combs is not cured by the disclosure of Nelson. Simply because Nelson may disclose X-ray imaging utilizing two different X-ray energy levels, there is no disclosure in Nelson of a method of imaging in wherein the distribution of bioluminescent and/or fluorescent markers is determined by separate detection of photons having a first average energy, which are emitted by the bioluminescent and/or fluorescent markers, by at least one first detector and wherein the distribution of radioactive markers is determined by simultaneous separate detection of photons having a second average energy, which are emitted by the radioactive markers, by at least one second detector, as required in the presently claimed invention. As Combs does not provide a method of imaging in any form, modification of this method with that of Nelson would not lead to the presently claimed invention. Furthermore, the method of Nelson relates to imaging utilizing two different X-ray energy levels, not a bioluminescent and/or fluorescent energy level and a radioactive energy, as recited in the presently claimed invention.

Applicant respectfully submits that the Examiner has not set forth a proper *prima facie* case of obviousness. In view of the foregoing remarks, Applicant respectfully requests reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a).

III. The Rejection of Claims 23 and 24 Under 35 U.S.C. § 103 Should be Withdrawn

Claims 23 and 24 have been rejected under 35 U.S.C. § 103(a), as allegedly being unpatentable over Combs in view of Nelson and further in view of U.S. Patent No. 6,757,554, to Rubinstein, *et al.* (hereinafter “Rubinstein”). Applicant respectfully traverses this rejection.

The Office Action suggests that Combs and Nelson disclose the present invention as set forth above. However, the Office Action concedes that the combination of Combs and Nelson fails to disclose a layer used to transmit or reflect photons according to their energy level. The Office Action attempts to cure this deficiency with the disclosure of Rubinstein, suggesting that Rubinstein discloses a filter. The Office Action concludes that it would have been obvious to provide a layer for each of the detectors in order to minimize background emissions and only allow the intended range of emission energies to pass. Applicant respectfully disagrees with these contentions and conclusions.

As set forth above, Applicant submits that Combs and Nelson do not disclose the presently claimed invention, as the combination of references fails to disclose the presently claimed method of imaging. Applicant submits that this deficiency is not cured by the disclosure of Rubinstein, as Rubinstein also does not disclose a method of imaging, let alone a method wherein the distribution of the bioluminescent and/or fluorescent markers is determined by separate detection of photons having a first average energy, which are emitted by the bioluminescent and/or fluorescent markers, by at least one first detector and wherein the distribution of the radioactive markers is determined by simultaneous separate detection of photons having a second average energy, which are emitted by the radioactive markers, by at least one second detector.

Furthermore, present claim 23 (and hence, claim 24 that depends ultimately therefrom), recites that in the step of determining *in vivo* distributions, the photons of the bioluminescent and/or fluorescent markers having the first average energy and the photons of the radioactive markers having the second average energy are separated for the separate detection with the aid of a layer, the layer essentially reflecting or transmitting the photons in a manner dependent on their energy. Contrary to the suggestions in the Office Action, Applicant asserts that the filter disclosed in Rubinstein is utilized to filter out specific wavelengths of light. *See* Rubinstein at

column 8, lines 48-50. There is no indication in Rubinstein that these filters would allow for separate reflection or transmission of photons of the bioluminescent and/or fluorescent markers having a first average energy and photons of the radioactive markers having a second average energy.

Furthermore, since only a concentration is to be measured in Rubinstein, only a single light intensity is provided by the photodetector. *See* Rubinstein at column 5, lines 41-49. Thus, the approach of Rubinstein is not compatible with imaging nor is it related to a distinct wavelength and, in particular, does not relate to light measurements concurrent with measurements of a radioactive marker. Instead, Rubinstein merely discloses clearance detection using light only. Thus, Rubinstein does not disclose the layers recited in present claims 23 and 24.

Applicant notes that if an independent claim is nonobvious under § 103, then any claim depending therefrom is nonobvious. *In re Fine*, 5 USPQ2d 1596 (Fed. Cir. 1988). *See* M.P.E.P. § 2143.03. Thus, Applicants submit that as claim 22 is nonobvious, claims 23 and 24, each of which ultimately depends from independent claim 22, are also non-obvious at least by virtue of their dependency from claim 22. Applicant respectfully submits that the Examiner has not set forth a proper *prima facie* case of obviousness. In view of the foregoing remarks, Applicant respectfully requests reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a).

IV. The Rejection of Claim 25 Under 35 U.S.C. § 103 Should be Withdrawn

Claim 25 has been rejected under 35 U.S.C. § 103(a), as allegedly being unpatentable over Combs in view of Nelson and further in view of U.S. Patent No. 6,232,107, to Bryan, *et al.* (hereinafter “Bryan”). Applicant respectfully traverses this rejection.

The Office Action suggests that Combs and Nelson disclose the present invention as set forth above. However, the Office Action concedes that the combination of Combs and Nelson fails to disclose the use of green fluorescent proteins (GFP). The Office Action attempts to cure this deficiency with the disclosure of Bryan, suggesting that Bryan discloses GFP. The Office Action concludes that it would have been obvious to utilize GFP in the combined method of Combs and Nelson. Applicant respectfully disagrees with these contentions and conclusions.

As set forth above, Applicant submits that Combs and Nelson do not disclose the presently claimed invention, as the combination of references fails to disclose the presently claimed method of imaging. Applicant submits that this deficiency is not cured by the disclosure of Bryan, as Bryan also does not disclose a method of imaging wherein the distribution of the bioluminescent and/or fluorescent markers is determined by separate detection of photons having a first average energy, which are emitted by the bioluminescent and/or fluorescent markers, by at least one first detector and wherein the distribution of the radioactive markers is determined by simultaneous separate detection of photons having a second average energy, which are emitted by the radioactive markers, by at least one second detector.

Applicant notes that if an independent claim is nonobvious under § 103, then any claim depending therefrom is nonobvious. *In re Fine*, 5 USPQ2d 1596 (Fed. Cir. 1988). *See* M.P.E.P. § 2143.03. Thus, Applicant submits that as claim 22 is nonobvious, claim 25, which ultimately depends from independent claim 22, is also non-obvious at least by virtue of its dependency from claim 22. Applicant respectfully submits that the Examiner has not set forth a proper *prima facie* case of obviousness. In view of the foregoing remarks, Applicant respectfully requests reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a).

V. The Rejection of Claim 26 Under 35 U.S.C. § 103 Should be Withdrawn

Claim 26 has been rejected under 35 U.S.C. § 103(a), as allegedly being unpatentable over Combs in view of Nelson and further in view of Published U.S. Patent Application No. 2003/0101466, to Turner (hereinafter “Turner”). Applicant respectfully traverses this rejection.

The Office Action suggests that Combs and Nelson disclose the present invention as set forth above. However, the Office Action concedes that the combination of Combs and Nelson fails to disclose detecting Indium-111 using SPECT. The Office Action attempts to cure this deficiency with the disclosure of Turner, suggesting that Turner discloses the use of SPECT to detect Indium-111. The Office Action concludes that it would have been obvious to utilize Indium-111 in the combined method of Combs and Nelson. Applicant respectfully disagrees with these contentions and conclusions.

As set forth above, Applicant submits that Combs and Nelson do not disclose the presently claimed invention, as the combination of references fails to disclose the presently claimed method of imaging. Applicant submits that this deficiency is not cured by the disclosure of Turner, as Turner also does not disclose a method of imaging wherein the distribution of the bioluminescent and/or fluorescent markers is determined by separate detection of photons having a first average energy, which are emitted by the bioluminescent and/or fluorescent markers, by at least one first detector and wherein the distribution of the radioactive markers is determined by simultaneous separate detection of photons having a second average energy, which are emitted by the radioactive markers, by at least one second detector.

Applicant notes that if an independent claim is nonobvious under § 103, then any claim depending therefrom is nonobvious. *In re Fine*, 5 USPQ2d 1596 (Fed. Cir. 1988). *See* M.P.E.P. § 2143.03. Thus, Applicant submits that as claim 22 is nonobvious, claim 26, which ultimately depends from independent claim 22, is also non-obvious at least by virtue of its dependency from claim 22. Applicant respectfully submits that the Examiner has not set forth a proper *prima facie* case of obviousness. In view of the foregoing remarks, Applicant respectfully requests reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a).

VI. The Rejection of Claim 27 Under 35 U.S.C. § 103 Should be Withdrawn

Claim 27 has been rejected under 35 U.S.C. § 103(a), as allegedly being unpatentable over Combs in view of Nelson and further in view of Turner and U.S. Patent No. 6,312,961, to Voirin *et al.* (hereinafter “Voirin”). Applicant respectfully traverses this rejection.

The Office Action suggests that Combs, Nelson and Turner disclose the present invention as set forth above. However, the Office Action concedes that the combination of Combs, Nelson and Turner fail to disclose detecting fluorescent markers using a CCD camera. The Office Action attempts to cure this deficiency with the disclosure of Voirin, suggesting that Voirin discloses the use of a CCD camera to detect fluorescent emissions. The Office Action concludes that it would have been obvious to utilize CCD camera to detect fluorescent emissions in the combined method of Combs, Nelson and Turner. Applicant respectfully disagrees with these contentions and conclusions.

As set forth above, Applicant submits that Combs, Nelson and Turner do not disclose the presently claimed invention, as the combination of references fails to disclose a method of imaging. Applicant submits that this deficiency is not cured by the disclosure of Voirin, as Voirin also does not disclose a method of imaging wherein the distribution of the bioluminescent and/or fluorescent markers is determined by separate detection of photons having a first average energy, which are emitted by the bioluminescent and/or fluorescent markers, by at least one first detector and wherein the distribution of the radioactive markers is determined by simultaneous separate detection of photons having a second average energy, which are emitted by the radioactive markers, by at least one second detector.

Applicant notes that if an independent claim is nonobvious under § 103, then any claim depending therefrom is nonobvious. *In re Fine*, 5 USPQ2d 1596 (Fed. Cir. 1988). *See* M.P.E.P. § 2143.03. Thus, Applicants submit that as claim 22 is nonobvious, claim 27, which ultimately depends from independent claim 22, is also non-obvious at least by virtue of its dependency from claim 22. Applicant respectfully submits that the Examiner has not set forth a proper *prima facie* case of obviousness. In view of the foregoing remarks, Applicant respectfully requests reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a).

VII. The Rejection of Claims 29 and 30 Under 35 U.S.C. § 103 Should be Withdrawn

Claims 29 and 30 have been rejected under 35 U.S.C. § 103(a), as allegedly being unpatentable over Combs in view of Nelson and further in view of Turner, Voirin and Rubinstein. Applicant respectfully traverses this rejection.

The Office Action suggests that Combs, Nelson, Turner and Voirin disclose the present invention as set forth above. However, the Office Action concedes that the combination of Combs, Nelson, Turner and Voirin fails to disclose the use of a filter. The Office Action attempts to cure this deficiency with the disclosure of Rubinstein, suggesting that Rubinstein discloses a filter. The Office Action concludes that it would have been obvious to utilize the filter of Rubinstein in the combined method of Combs, Nelson, Turner and Voirin. Applicant respectfully disagrees with these contentions and conclusions.

As set forth above, Applicant submits that Combs, Nelson, Turner, Voirin and Rubinstein do not disclose the presently claimed invention, as the combination of references fails to disclose the presently claimed method of imaging. Applicant submits that this deficiency is not cured by the disclosure of Rubinstein, as Rubinstein also does not disclose a method of imaging wherein the distribution of the bioluminescent and/or fluorescent markers is determined by separate detection of photons having a first average energy, which are emitted by the bioluminescent and/or fluorescent markers, by at least one first detector and wherein the distribution of the radioactive markers is determined by simultaneous separate detection of photons having a second average energy, which are emitted by the radioactive markers, by at least one second detector.

Applicant notes that if an independent claim is nonobvious under § 103, then any claim depending therefrom is nonobvious. *In re Fine*, 5 USPQ2d 1596 (Fed. Cir. 1988). *See* M.P.E.P. § 2143.03. Thus, Applicants submit that as claim 22 is nonobvious, claims 29 and 30, which ultimately depend from independent claim 22, are also non-obvious at least by virtue of their dependency from claim 22. Applicant respectfully submits that the Examiner has not set forth a proper *prima facie* case of obviousness. In view of the foregoing remarks, Applicant respectfully requests reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a).

VIII. The Rejection of Claims 31-34 and 36-41 Under 35 U.S.C. § 103 Should be Withdrawn

Claims 31-34 and 36-41 have been rejected under 35 U.S.C. § 103(a), as allegedly being unpatentable over Combs in view of Nelson and further in view of Turner, Voirin, Rubinstein and further in view of U.S. Patent No. 5,647,363 to Rabito *et al.* (hereinafter “Rabito”). Applicant respectfully traverses this rejection.

The Office Action suggests that Combs, Nelson, Turner, Voirin and Rubinstein disclose the present invention as set forth above. However, the Office Action concedes that the combination of Combs, Nelson, Turner, Voirin and Rubinstein fails to disclose the different configurations and arrangements of the SPECT and CCD cameras. The Office Action attempts to cure this deficiency with the disclosure of Rabito, suggesting that Rabito discloses the recited arrangement.

As set forth above, Applicant submits that Combs, Nelson, Turner, Voirin and Rubinstein do not disclose the presently claimed invention, as the combination of references fails to disclose the presently claimed method of imaging. Applicant submits that this deficiency is not cured by the disclosure of Rabito, as Rabito also does not disclose a method of imaging wherein the distribution of the bioluminescent and/or fluorescent markers is determined by separate detection of photons having a first average energy, which are emitted by the bioluminescent and/or fluorescent markers, by at least one first detector and wherein the distribution of the radioactive markers is determined by simultaneous separate detection of photons having a second average energy, which are emitted by the radioactive markers, by at least one second detector.

Applicant notes that if an independent claim is nonobvious under § 103, then any claim depending therefrom is nonobvious. *In re Fine*, 5 USPQ2d 1596 (Fed. Cir. 1988). *See* M.P.E.P. § 2143.03. Thus, Applicant submits that as claim 22 is nonobvious, claims 31-34 and 36-41, which ultimately depend from independent claim 22, are also non-obvious at least by virtue of their dependency from claim 22. Applicant respectfully submits that the Examiner has not set forth a proper *prima facie* case of obviousness. In view of the foregoing remarks, Applicant respectfully requests reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a).

IX. The Rejection of Claim 35 Under 35 U.S.C. § 103 Should be Withdrawn

Claim 35 has been rejected under 35 U.S.C. § 103(a), as allegedly being unpatentable over Combs in view of Nelson and further in view of Turner, Voirin, Rubinstein, Rabito and further in view of Published U.S. Patent Application No. 2002/0042566 to Matsuzaki *et al.* (hereinafter “Matsuzaki”). Applicant respectfully traverses this rejection.

The Office Action suggests that Combs, Nelson, Turner, Voirin, Rubinstein and Rabito disclose the present invention as set forth above. However, the Office Action concedes that the combination of Combs, Nelson, Turner, Voirin, Rubinstein and Rabito fails to disclose the use of a position sensor. The Office Action attempts to cure this deficiency with the disclosure of Matsuzaki, suggesting that Matsuzaki discloses the use of a positions sensor.

As set forth above, Applicant submits that Combs, Nelson, Turner, Voirin, Rubinstein and Rabito do not disclose the presently claimed invention, as the combination of references fails to disclose the presently claimed method of imaging. Applicant submits that this deficiency is

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not cured by the disclosure of Matsuzaki, as Matsuzaki also does not disclose a method of imaging wherein the distribution of the bioluminescent and/or fluorescent markers is determined by separate detection of photons having a first average energy, which are emitted by the bioluminescent and/or fluorescent markers, by at least one first detector and wherein the distribution of the radioactive markers is determined by simultaneous separate detection of photons having a second average energy, which are emitted by the radioactive markers, by at least one second detector.

Applicant notes that if an independent claim is nonobvious under § 103, then any claim depending therefrom is nonobvious. *In re Fine*, 5 USPQ2d 1596 (Fed. Cir. 1988). See M.P.E.P. § 2143.03. Thus, Applicants submit that as claim 22 is nonobvious, claim 35, which ultimately depends from independent claim 22, is also non-obvious at least by virtue of its dependency from claim 22. Applicant respectfully submits that the Examiner has not set forth a proper *prima facie* case of obviousness. In view of the foregoing remarks, Applicant respectfully requests reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a).

X. New Claims 42 and 43

Applicant respectfully submits, for at least the reasons set forth above, newly added claims 42 and 43 are also nonobvious in view of the references cited in the Office Action.

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XI. Conclusion

Applicants believe that the claims are in condition for allowance and respectfully request allowance thereof. The Examiner is invited to telephone the undersigned if that would be helpful in resolving any issues.

It is not believed that extensions of time or fees for net addition of claims are required beyond those that may otherwise be provided for in documents accompanying this paper. However, if additional extensions of time are necessary to prevent abandonment of this application, then such extensions of time are hereby petitioned under 37 C.F.R. § 1.136(a), and any fees required therefor (including fees for net addition of claims) are hereby authorized to be charged to our Deposit Account No. 50-5071.

Respectfully submitted,

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